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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,212	01/04/2002	John Colyer	10069/1004	6487

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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/037,212

Applicant(s)

COLYER ET AL.

Examiner

Michael Borin

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2004.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38,40-52 and 91 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 38,40-52 and 91 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Status of Claims

Acknowledgement is made of the amendment filed 11/18/2004. Claims 1-37,39,53-90 are canceled. Claims 38,40-52,91 are pending.

Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn. The following rejections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, second paragraph.

Claims 38,40-52,91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons:

Claim 38 is amended to recite that the reporter molecule and the binding partner interact in a "coiled-coil manner". The term "associate in coiled-coil manner" is vague and unclear; it does not define the scope of interactions (associations) encompassed by the claims. The teaching of specification ranges from admitting (p. 7, bottom) that binding partner may not have coiled-coil if it is not needed for binding (then, what constitutes association in a coiled-coil manner?) to suggesting that the reporter molecule has two coiled-coils and self associates (then, what is the binding partner?).

Applicants refer to Declaration of Dr. Woolfson which states that the "coiled-coil proteins of the instant application comprise a stable, inert background structure". However, the instant claims are not limited to any particular proteins;

rather, they encompass any agents that, associate in "a coiled-coil dependent manner".

Claim Rejections - 35 USC § 103.

Claims 38, 40,45,49-52,91 are rejected under 35 U.S.C. 103(a) as obvious over Tsien et al (US Patent 6197928).

Tsien et al teach method for determining the concentration of an analyte in a sample using a fluorescently labeled peptide comprising a binding protein moiety having an analyte-binding domain which binds an analyte, a donor fluorescent protein moiety covalently coupled to the binding protein moiety, and an acceptor fluorescent protein moiety covalently coupled to the binding protein moiety. Analyte binding to the analyte binding domain causes a conformational change in the analyte binding domain, which in turn induces conformational changes in the position or orientation of the donor fluorescent protein and acceptor fluorescent protein moieties with respect to one another, thereby altering the relative amounts of fluorescence from the two fluorescent protein moieties when the donor is excited by irradiation. See claim 24. The binding is measured by energy transfer, FRET, using two fluorescent labels (claims 19,25-27) . In FRET, the "donor fluorescent protein moiety" and the "acceptor fluorescent protein moiety" are selected so that the donor and acceptor moieties exhibit fluorescence resonance energy transfer when the donor moiety is excited. The binding protein moiety can be a kinase (claim 11).

Although the referenced claims are not drawn to "monitoring activity of an enzyme", such as kinase, as instantly claimed, it would be *prima facie* obvious to one skilled in the art that, as a kinase is one of the possible enzymes used in the

method, the method can be used to monitor phosphorylating activity of a kinase (i.e., activity resulting in an attachment of a phosphate moiety).

In regard to "site sufficient for the addition of [phosphate] moiety", every protein actin contains a plurality of residues suitable for addition of a phosphate moiety (e.g., Ser, Thr, Tyr, His, and Lys residues).

In regard to term "non-natural" the term refers to way of preparing the claimed compound rather than distinguishes it structurally from products obtained otherwise. It is the novelty and patentability of the product used in the instant method that need to be established and not that of the process of making steps.

Applicant argues that Tsien et al. reference does contain any teaching about coiled-coil proteins, and, therefore, does not teach binding in a coiled-coil dependent manner. Examiner agrees that the reference broadly describes the method and is silent about particular details of spatial organization of interacting proteins. However, the fact that the reference is silent about the presence of coiled-coil structures in the described method does not indicate that such structures would be inoperable in the referenced method. Contrary, it is known that protein kinases can contain coiled-coil structures¹, and/or interact with other agents² in a coiled-coil dependent manner. Therefore, Examiner can not exclude that the proteins described in the referenced method do not comprise coiled-coil

¹ See Zhang et al. (Database Caplus, DN 139:226410. FEBS Letters (2003), 546(2-3), 281-287) and Ishizaki et al. (Database Caplus, DN 126:249258. FEBS Letters (1997), 404(2,3), 118-124) demonstrating presence of coiled-coil in different protein kinases.

² See Gillingham et al. (Database Caplus, DN 135:72954. EMBO Reports (2000), 1(6), 524-529) demonstrating binding to protein kinase A in coiled-coil-dependent manner.

structures and/or are clearly incapable of interacting in coiled-coil dependent manner. Since the Office does not have the facilities for examining proteins addressed in the prior art, the burden is on applicant to show that these proteins do not comprise coiled-coil structures and/or clearly incapable of interacting in coiled-coil dependent manner. See *In re Best*, 562 F.d. 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. Furthermore, note that the specification, teaches that coiled-coil is not absolutely required for binding; this structural element is not required if the binding may occur without it – see p. 7, bottom.

Further, applicant argues that Examiner ignores limitation of “non-natural site” required to be present in the polypeptide which binds the phosphate moiety. The term “non-natural” fails to patentably distinguish structure of polypeptide used in the invention from any other synthetic polypeptide. As discussed in specification, once the polypeptide is “engineered” (which Examiner reads as “synthesized”), it is no longer naturally occurring (see specification, paragraph bridging pages 8 and 9). Thus, the term “non-natural”, same as term “engineered”, refers to way of preparing the claimed compound, rather than distinguishes it structurally from products obtained otherwise. Further, as discussed in specification, the site for interacting with a moiety does not necessarily have to contain engineered (or non-natural) part – see specification, p. 7, bottom.

Further, applicant asserts that there would be no motivation to utilize the measurements of amount of polypeptide, kinase for example, in monitoring its activity. Note, however, that the disclosure of the reference begins from discussion that ‘measurement of an analyte concentration ... can help elucidate the physiological function of the analyte’. See col. 1, lines 14-16. In the case of a

kinase, the physiological function would be its enzymatic activity; hence, Examiner maintains that it would be obvious to employ the referenced method in monitoring of enzymatic activity.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571)272-0713. The examiner can normally be reached on 9 am-5 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 Michael Borin
Primary Examiner
Art Unit 1631

mlb